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13. ABSTRACT (Maximum 200 Words)

Metastatic lesions in the proximal femur are a common and serious manifestation of breast cancer. These lesions can be painful and can lead to pathological fracture. Prophylactic surgical fixation is advised in patients thought to be at high risk of fracture and typically involves placement of a prosthetic implant or compression hip screw. This study is investigating whether proximal femora with metastatic lesions can be repaired by simply filling the defect with bone cement (polymethylmethacrylate), an innovative procedure that could be performed percutaneously and could eliminate the need for implanting hardware in many cases. If defects could be repaired using this technique, patients would benefit from shorter and less invasive surgical procedures, less pain and discomfort, greatly reduced recovery time, and shorter hospital stays – all at much lower cost. To date, mechanical testing and finite element modeling of femora with and without repaired simulated tumors support the feasibility of this repair technique. The finite element modeling method has been calibrated to produce accurate estimates of measured fracture load and validated on an independent data set. This method is being used to develop clinical guidelines for assessing the need for prophylactic fixation and for using the proposed percutaneous repair procedure.

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Introduction

Metastatic lesions in the proximal femur are a common and serious manifestation of breast cancer. These lesions can be painful and can lead to pathological fracture. Prophylactic surgical fixation is advised in those patients thought to be at high risk of fracture and typically involves placement of a prosthetic implant or a compression hip screw to provide strength. In this study, we are investigating whether proximal femora with metastatic lesions can be repaired by simply filling the defect with bone cement (polymethylmethacrylate), an innovative procedure that could be performed percutaneously and could eliminate the need for implanting hardware in many cases. If the metastatic defect could be safely repaired using this new technique, the patient would benefit from a shorter and less invasive surgical procedure, less pain and discomfort, greatly reduced recovery time, and a shorter hospital stay—all at much lower cost. Using finite element (FE) analysis, this study will also develop clinical guidelines both for assessing the need for prophylactic fixation and for using the proposed percutaneous surgical procedure. This extensive evaluation will enable rapid and safe clinical implementation of the new repair technique and surgical guidelines via a clinical trial immediately following this study.

Body

During Year 1 of this study, [Task 1a] 12 matched pairs of cadaveric proximal femora were obtained and [Task 1b] a roughly spherical defect was introduced into one randomly selected proximal femur from each pair. [Task 1c] After identifying and obtaining the necessary equipment and supplies, the defects in the femora were repaired using the proposed repair technique. [Task 1e] The mechanical properties of bone cement in tension and compression were obtained from the extensive available literature (Saha and Paul, 1984). After the defects were

repaired, [Task 1d] all 24 bones were CT scanned and [Task 1g] the bones were mechanically tested to failure. Using the data for the intact bones, the existing finite element modeling method (Keyak, 2001), which previously systematically overestimated the measured fracture load, was calibrated and validated. That is, to improve model accuracy, the relationships used to calculate mechanical properties for the FE models were modified until the resulting relationship between the measured and predicted fracture loads was approximately 1:1, with slope and intercept not significantly different from one and zero, respectively. After calibration was complete, [Task 1f] FE models of the 12 intact femora obtained in Task 1a were created from the CT scan data and compared with the mechanical testing data, and thereby served as an independent data set on which to validate the calibrated modeling method. These results have been presented to the Orthopaedic Research Society and are currently being prepared for journal publication.

With the newly calibrated FE modeling method, [Task 1f] FE models of the 12 repaired bones gathered in Task1a were created from the CT scan data. The femora with the repaired defects included mechanical properties for bone cement, as obtained in Task 1e. One pair of femora was removed from data analysis after the repaired femur from the pair was discovered to have a fracture prior to mechanical testing.

[Task 1h, 1i] To assess the feasibility of the surgical procedure, measured %intact was calculated for each matched pair of specimens as the measured fracture load for the repaired femur divided by the measured fracture load for the contralateral intact femur. The mean and standard deviation (SD) of measured %intact were 94.7% and 8.7%, respectively, indicating that 99.8% of the population would have a measured %intact greater than 70%, and 95.5% of the population would have a measured %intact greater than 80%. These strong results clearly support the feasibility of the percutaneous repair technique.

Analysis of variance (ANOVA) showed that measured %intact does not depend on defect site ($p > 0.2$), although the power to detect such a difference was low (17%). Therefore, no strong conclusions can be made in this regard.

[Task 1j] Validity of the FE models of the repaired femora was assessed by performing simple linear regression analysis between F_{Meas} (N) and F_{FE} (N) for the intact and repaired femora (Fig. 1) and comparing results: intact, $F_{Meas} = 1710 + 0.888F_{FE}$, $p < 0.001$, $R = 0.89$; repaired, $F_{Meas} = 1038 + 0.913F_{FE}$, $p < 0.001$, $R = 0.94$. The slope and intercept for both equations are not significantly different from one and zero, respectively. Thus, the FE models of the repaired femora are valid. [Task 1k] Therefore, further modification of the FE modeling procedure is not necessary.

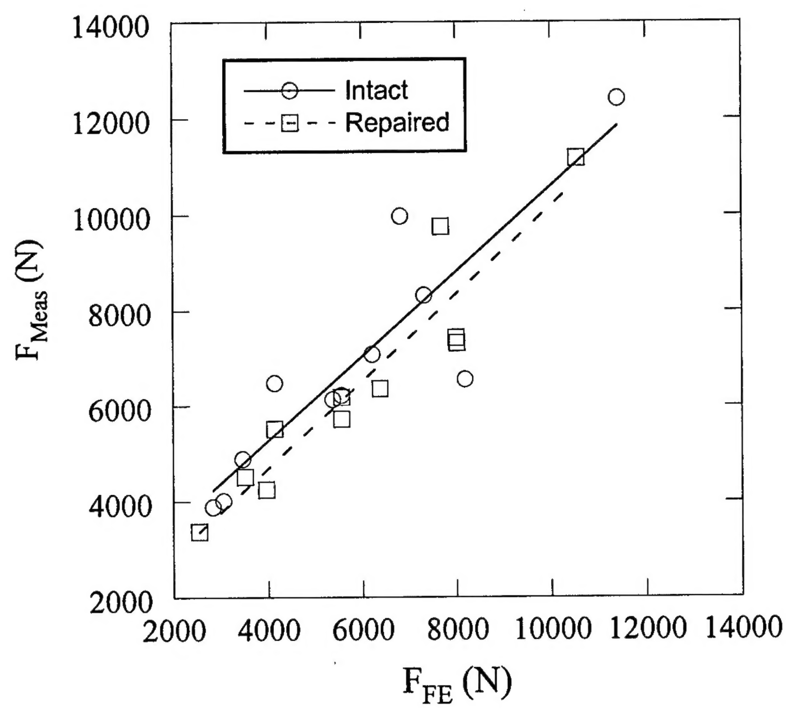

Fig. 1. F_{Meas} versus F_{FE} for the intact and repaired femora.

The predicted %intact was calculated for each matched pair of specimens as the FE-

predicted fracture load for the repaired femur divided by the FE-predicted fracture load for the contralateral intact femur. The ability of the FE models to predict measured %intact was quantified by calculating the difference between measured %intact and predicted %intact (measured %intact – predicted %intact) for each donor (mean = -8.9%, standard deviation = 11.1%). Thus, the FE models tended to overstate measured %intact by an average of 8.9%. This finding is consistent with the fact that regions in which the bone cement penetrated into the trabecular bone were modeled as bone cement alone, rather than as a mixture of bone cement and trabecular bone, so the material properties in these areas were overstated. Because the computer models used later in this study will not allow for cement penetration into the trabecular bone, these models will not tend to overstate the mechanical properties, and may in fact tend to understate the strength of the surgical result (i.e. a conservative assessment of strength).

[Task 2a] Computer programs have been written to model simulated metastatic defects at any location within the proximal femur FE models and to model the drill hole created when repairing these defects using the proposed percutaneous technique. When the FE models are used to simulate repair, the defect and drill hole are assigned the mechanical properties of bone cement.

[Tasks 2b and 2c] To date, several hundred FE models have been created simulating the introduction and repair of metastatic defects in femora under single-limb stance type loading. For static loading (single load to failure), it is apparent that the proposed repair technique successfully restores the strength of the bone to its intact state, even after accounting for potential inaccuracies of the FE models, no matter the defect size or location. Additionally, defects located on the inferior-medial aspect of the proximal femur neck appear to cause the most significant decreases in femur strength but still can be adequately repaired with this technique. Hence, there

does not appear to be a critical defect size beyond which the repair technique cannot be used for short term or low cyclic loading situations (i.e. for patients who are bedridden, who are wheel-chair bound, or who have short life expectancies). However, it appears that not all defect sizes and locations repaired with this technique can be restored to achieve adequate fatigue strength (strength under cyclic loading). Evaluation in this area is continuing. Final clinical guidelines for the use of the new repair technique will incorporate these observations and will be developed with the use of statistical tools.

Key Research Accomplishments

- Surgical instruments and supplies needed for the proposed repair technique were identified and obtained.
- FE modeling method was calibrated to provide accurate estimates of measured fracture load.
- Measured %intact (mean = 94.7%, SD = 8.7%) clearly supports feasibility of percutaneous repair technique.
- Measured and computed fracture loads for intact and repaired femora indicate that the FE models are valid for evaluating the proposed repair technique.
- Computer programs have been developed to simulate metastatic defects and the percutaneous repair technique within the FE models.
- Feasibility of the proposed minimally invasive repair technique is indicated, at a minimum, for low cyclic loading situations.

Reportable Outcomes

Kaneko TK, Keyak JH: Calibration and validation of finite element models for predicting proximal femoral fracture load. Trans Orthop Res Soc 29, 521, 2004. [abstract]

Keyak JH, Skinner HB, Kaneko TS, and Armstrong KL: Percutaneous repair of proximal femora with metastatic lesions. Department of Orthopaedic Surgery Graduate Research Forum, University of California, Irvine, CA, 5/30/03. [podium presentation]

Kaneko TK, Keyak JH: Calibration and validation of finite element models for predicting proximal femoral fracture load. Orthopaedic Research Society, 50th Annual Meeting, San Francisco, CA, 3/7-10/04. [poster presentation]

Kaneko TK, Keyak JH: Calibration and validation of finite element models for predicting proximal femoral fracture load. College of Medicine Faculty Research Poster Session, University of California, Irvine, CA, 3/24/04. [poster presentation]

Conclusions

Conventional surgery to prevent pathological fracture, involving implantation of hardware, is highly invasive. If this study shows that a metastatic defect can be safely repaired percutaneously by simply filling the defect with bone cement, <u>the patient would benefit from a shorter and less invasive surgical procedure with less pain and discomfort, greatly reduced recovery time, and shorter hospital stay – all at much lower cost.</u>

The decision to perform prophylactic fixation is complicated by the inadequacy of tools

for identifying patients in need of fixation (Hipp et al., 1995). This study is attempting to address this issue by providing surgical guidelines based on the structural deficit caused by the lesion. More significantly, the availability of a minimally-invasive alternative to traditional surgical fixation will reduce the reluctance to perform surgical repair in those cases where the need for intervention is unclear.

Results to date indicate that the proposed minimally invasive procedure may be a viable option for, at a minimum, situations with low cyclic loading, such as for patients who are bedridden, who are wheel chair bound, or who have short life expectancies.

References

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